

Amendments to the Specification:

Please add the following paragraph between the title and the first line of text as follows:

This application is a national stage application of International Application No. PCT/IB2004/002433, filed July 29, 2004, which claims the benefit of U.S. Provisional Application No. 60/490,946, filed July 30, 2003.

Please amend the following paragraphs that were directed to be added after the paragraph ending on page 3, line 27, in the January 21, 2010 Amendment:

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 represents a coding DNA sequence and corresponding polypeptide sequence according to the invention.

Figure 2A represents amino acids ~~545-684~~540 to 679 (SEQ ID NO:1) of the gp160 envelope protein of HIV. The sequence is taken from a consensus sequence of 32 strains in the Swissprot database and is identical with the sequence of isolate ENV_HV1BR (Swiss-Prot P03377).

Figure 2B represents peptide sequences (SEQ ID NOs:3-6, their numbering corresponding to Figure 2A) of regions where structural analogies or homologies with IL-2 are present.

Figure 2C represents a linker oligopeptide (SEQ ID NO:2) convenient for linking the N- and C- terminal peptides of gp41 after removal of amino acids ~~604-615~~599 to 610 or ~~598-622~~593 to 617 of the gp160 envelope protein of HIV of Figure 2A.

Figure 2D represents oligopeptide sequences (SEQ ID NOs:15 and 16, their numbering corresponding to Figure 2A) that may be advantageously replaced by a linker in accordance with the invention.

Figure 3 represents amino acids ~~539-675~~ 540 to 675 (SEQ ID NO:14) and the corresponding nucleotide sequence (SEQ ID NO:13) of the gp160 envelope protein of HIV. The sequence is taken from the reference strain HxB2 gp41, where amino acids 598 and 604 have been replaced with serine.

Figures 4A and 4B represent sequences (SEQ ID NOs:17 and 18) of two representative polypeptides according to the invention.

Figures 5A and 5B represent sequences (SEQ ID NOs:19 and 20) of two representative polypeptides according to the invention.

Figure 6 represents a polypeptide sequence (SEQ ID NO:21) illustrating the invention, with N-terminal truncation, and comprising the linker sequence of Figure 2C (SEQ ID NO:2).

Figure 7 represents the primer sequences used in the amplification of the gp41 N-helix and the introduction of the linker (SEQ ID NOs:9 and 10) and for the amplification of the C-helix (SEQ ID NOs:11 and 12).

Figure 8 is a chromatographic elution profile of the polypeptide of the invention on a Superdex 200 HR liquid chromatography column.

DETAILED DESCRIPTION OF EMBODIMENTS

Please replace the paragraph beginning on page 4, line 3, with the following rewritten paragraph:

Within another embodiment of the invention, the deleted wildtype oligopeptide is located in the region from ~~598 to 622~~ 593 to 617, in particular in the region from ~~603 to 615~~ 599 to 610 of the gp41 protein, according to the numbering of SEQ ID NO 1 ~~(Fig. 2A)~~ in Figure 2A.

Please replace the paragraph beginning on page 4, line 6, with the following rewritten paragraph:

Within another embodiment of the invention, the deleted oligopeptide is located in the region from ~~593 to 617~~ 55 to 79, in particular in the region from ~~599 to 610~~ 61 to 72, according to the numbering of SEQ ID NO 14 (Fig. 3).

Please replace the paragraph beginning on page 4, line 31, with the following rewritten paragraph:

The peptide sequence ~~545-684~~ 540 to 679 (SEQ ID NO:1), reproduced in Figure 2A, is a gp41 consensus sequence of 32 HIV-1 strains in the Swiss Protein Database. This sequence is identical with the sequence of isolate ENV_HV1BR (Swiss-Prot P03377).

Please replace the paragraph beginning on page 6, line 24, with the following rewritten paragraph:

Wildtype oligopeptides that may be advantageously replaced by a linker in accordance with the present invention are represented by SEQ ID NO 15 and SEQ ID NO 16 (Figure 2D). These correspond respectively to amino acids ~~to 604 to 615~~ 599 to 610, and ~~598 to 622~~ 593 to 610 of SEQ ID NO 1 as numbered in Figure 2A, and to amino acids ~~599 to 610~~ 61 to 72 and ~~593 to 617~~ 55 to 79 of SEQ ID NO 14.

Please replace the paragraph beginning on page 7, line 4, with the following rewritten paragraph:

In the appended Figure 2B, the peptide sequences of four regions of this region of gp41 ~~555-557~~ 550 to 572 (SEQ ID NO 3), ~~572-601~~ 567 to 596 (SEQ ID NO 4), ~~590-620~~ 585 to 615 (SEQ ID NO 5) and ~~628-663~~ 623 to 658 (SEQ ID NO 6), are represented in which

structural analogies and/or cross reactions were noted with IL-2. These regions are homologously found in the SEQ ID NO 14, and respectively correspond to the peptide sequences found in positions ~~550-572, 567-597, 585-615, and 623-658~~ 12 to 34, 29 to 58, 47 to 77, and 85 to 120.

Please replace the paragraph beginning on page 8, line 1, with the following rewritten paragraph:

A modified polypeptide according to the instant invention is in particularly represented by the sequence SEQ ID NO 8 of Figure 1. This modified polypeptide has been derived from SEQ ID NO 14, wherein the oligopeptide sequence from positions 599-610 has been replaced with a linker corresponding to SEQ ID NO 2 (Figure 2C), and the oligopeptide sequence from positions 665-675 has been replaced by a His-Tag. In these sequences, an additional mutation has been carried-out in position ~~596-58~~ (numbering according to SEQ ID NO 14), wherein a tryptophan residue has been replaced by an aspartate amino acid residue.

Please replace the paragraph beginning on page 9, line 1, with the following rewritten paragraph:

As a particular embodiment of such modifications, mention may be made of amino acid mutation, as for example changing the tryptophan residue in position ~~528-58~~ (numbering of SEQ ID NO 14) by a more hydrophilic amino acid residue, such as an aspartate.

Please replace the paragraph beginning on page 9, line 5, with the following rewritten paragraph:

Other similar mutations are illustrated by the gp41 modified polypeptides set forth in SEQ ID NO 17 and SEQ ID NO 19 wherein the tryptophan in position 124 in SEQ ID NO 17

and 130 in SEQ ID NO 19, that would correspond to the tryptophan in position ~~685-680~~ of SEQ ID NO (not represented in this sequence), has been exchanged by an aspartate.

Please replace the paragraph beginning on page 11, line 21, with the following rewritten paragraph:

These oligonucleotide primers were designed to respectively introduce the sites for restriction enzymes NdeI and BamHI (twice underlined into the oligonucleotides primers sequences above). The sequences homologous to the gp41 gene in both oligonucleotide primers are written in italics. The oligonucleotide primer gp41-BamII was also designed to introduce (1) the oligopeptide linker SGGRGGS (SEQ ID NO 2) to replace the deleted portion of the loop (corresponding to the once and twice underlined sequences) and (2) a mutation at position ~~596-58~~ (protein numbering SEQ ID NO 14), where a tryptophan has been replaced by an aspartate amino acid (bold triplet).